

**REMARKS**

**Formal Matters**

Claims 1-10 and 33-42 are pending after entry of the amendments set forth herein.

Claims 1-10 and 33-42 were examined. Claims 1-10 and 33-42 were rejected.

Claims 1 and 42 are amended to specify that the flavin agent is present at a molar ratio of about 0.02 to about 17. Claim 33 has been amended to remove reference to the flavin agent in view of the above-described amendment to claim 1. The amendments to these claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim.

New matter has been added by these amendments. Accordingly, Applicants respectfully request entry thereof.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

**Rejections under 35 U.S.C. §102- Ouyang**

Claims 1, 2, 4-10 and 35-42 are rejected under 35 U.S.C. §102(a) as anticipated by Ouyang. As noted above, independent claims 1 and 42, and the claims that depend therefrom, have been amended to specify that the flavin agent is present at a molar ratio of about 0.02 to about 17. As Ouyang does not teach a flavin agent present at a molar ratio of about 0.02 to about 17, Applicants respectfully submit that Claims 1, 2, 4-10 and 35-42 are not anticipated by Ouyang for at least this reason. As such, Applicants respectfully request that this rejection be withdrawn.

**Rejections under 35 U.S.C. §102- Nippon Chemiphar**

Claims 1, 2, 4, 5, 8, 9, 35, 36, 39 and 40 are rejected under 35 U.S.C. §102(b) as anticipated by Nippon Chemiphar. As noted above, independent claim 1, and the claims that depend therefrom, has been amended to specify that the flavin agent is present at a molar ratio of about 0.02 to about 17. However, Nippon Chemiphar does not teach a flavin agent present at a molar ratio of about 0.02 to about 17, and as such does not anticipate claim 1 and the claims that for at least this reason.

In regards to claims 35, 36 39 and 40 indicated as rejected in the Final Office Action, Applicants note that the dependency of these claims was amended in Applicants' amendment and response filed January 20, 2004, such that these claims depend directly or indirectly from independent claim 34, which claim is not rejected under 35 U.S.C. §102(b) as anticipated by Nippon Chemiphar. Accordingly, Applicants believe the rejection of claims 35, 36 39 and 40 under 35 U.S.C. §102(b) as anticipated by Nippon Chemiphar should be withdrawn and request the Examiner to clarify the status of claims 35, 36 39 and 40 in the next communication.

For at least the reasons described above, the Applicants respectfully request this rejection be withdrawn.

**Rejections under 35 U.S.C. §102- Steinbach**

Claims 1, 2, 4, 6, 8, 35, 37, 39 are rejected under 35 U.S.C. §102(b) as anticipated by Steinbach. The Applicants respectfully traverse this rejection. As noted above, independent claim 1, and the claims that depend therefrom, has been amended to specify that the flavin agent is present at a molar ratio of about 0.02 to about 17. However, Steinbach does not teach a flavin agent present at a molar ratio of about 0.02 to about 17, and as such does not anticipate claim 1 and the claims that for at least this reason.

In regards to claims 35, 37 and 39 indicated as rejected in the Final Office Action, Applicants note that the dependency of these claims was amended in Applicants' amendment and response filed January 20, 2004, such that these claims depend directly or indirectly from independent claim 34, which claim is not rejected under 35 U.S.C. §102(b) as anticipated by Steinbach. Accordingly, Applicants believe the rejection of claims 35, 37 and 39 under 35 U.S.C. §102(b) as anticipated by Steinbach should be withdrawn and request the Examiner to clarify the status of claims 35, 37 and 39 in the next communication.

For at least the reasons described above, the Applicants respectfully request this rejection be withdrawn.

**Rejection under 35 U.S.C. §103 – Nippon and Geisler**

Claims 1-10 and 33-42 are rejected under 35 U.S.C. §103(a) as unpatentable in view of Nippon and Geisler. Applicants respectfully traverse this rejection.

The Advisory Action indicates, “Absent any evidence of the argued unexpected advantage or results, the claims remain rejected under 103.” However, Applicants respectfully submit that such evidence was provided in Applicants amendment and response filed January 20, 2004, responsive to the Final Office Action dated October 17, 2003.

Specifically, in that response, Applicants submitted that the compositions possess an unexpected property, i.e., stability, that is not fairly taught or suggested in the cited art, and directed the Examiner’s attention to specific parts of the instant specification that clearly evidence the unexpected properties. For example, these unexpected properties are best seen in Figs 1-3 of the instant application, where results show that the claimed compositions are unexpectedly stable at 56°C for one week. Figures 1, 2 and 3 respectively show that the presence of a borax, FAD, and borax and FAD dramatically increase the stability of a signal producing system over a signal producing system in the absence of FAD.

Accordingly, while the Advisory Action indicates that evidence to support these unexpected results has not been provided, Applicants respectfully submit that such evidence has been provided and in fact Applicants have directed the Examiner to the exact parts of the instant application where such evidence may be found. As such, Applicants respectfully submit that evidence of unexpected results has been provided. Because evidence of unexpected results has been provided, if this rejection is to be maintained Applicants respectfully request the Examiner to specify why the Examiner believes the submitted evidence is insufficient.

Finally, as noted in Applicants’ previous filed response, the Office has attempted to establish these rejections by arguing that “at the time of the claimed invention it would have been well within the purview of one of ordinary skill in the art to optimize amounts of effective ingredients as a matter of routine experimentation” and “one of skill in the art would have been motivated by routine practice to optimize the reagents of ... with a reasonable expectation for successfully obtaining an effective reagent composition.” However, the Office has not stated what would motivate one of skill in the art to add such

large amounts of flavin/group III compounds to the prior art compositions and then test those compositions for increased stability. Without such motivation, Applicants respectfully ask why one of skill in the art would produce the claimed invention by routine experimentation? If this rejection is to be maintained, for the record, the Applicants again respectfully request that the Examiner address this point specifically.

The Applicants respectfully submit that this rejection of the claims under 35 U.S.C. §103 has been adequately addressed. Withdrawal of this rejection is respectfully requested.

#### **Rejection under 35 U.S.C. §103 – Ouyang**

Claims 1-2, 4-10, 33 and 35-41 are rejected under 35 U.S.C. §103(a) as unpatentable in view of Ouyang. The Applicants respectfully traverse this rejection.

The Advisory Action indicates, “Absent any evidence of the argued unexpected advantage or results, the claims remain rejected under 103.” However, Applicants respectfully submit that such evidence was provided in Applicants amendment and response filed January 20, 2004, responsive to the Final Office Action dated October 17, 2003.

Specifically, in that response, Applicants submitted that the compositions possess an unexpected property, i.e., stability, that is not fairly taught or suggested in the cited art, and directed the Examiner’s attention to specific parts of the instant specification which clearly evidence the unexpected properties. For example, these unexpected properties are best seen in Fig. 2 of the instant application, where results show that the claimed compositions are unexpectedly stable at 56°C for one week. Figure 2 shows that the presence of FAD dramatically increase the stability of a signal producing system over a signal producing system in the absence of these compounds.

Accordingly, while the Advisory Action indicates that evidence to support these unexpected results has not been provided, Applicants respectfully submit that such evidence has been provided and in fact have directed the Examiner to the exact parts of the instant application where such evidence may be found. As such, Applicants respectfully submit that evidence of unexpected results has been provided. Because evidence of unexpected results has been provided, if this rejection is to be

maintained Applicants respectfully request the Examiner to specify why the Examiner believes the submitted evidence is insufficient.

Finally, as noted in Applicants' previous filed response, the Office has attempted to establish these rejections by arguing that "at the time of the claimed invention it would have been well within the purview of one of ordinary skill in the art to optimize amounts of effective ingredients as a matter of routine experimentation" and "one of skill in the art would have been motivated by routine practice to optimize the reagents of ... with a reasonable expectation for successfully obtaining an effective reagent composition." However, the Office has not stated what would motivate one of skill in the art to add such large amounts of flavin/group III compounds to the prior art compositions and then test those compositions for increased stability. Without such motivation, Applicants respectfully ask why one of skill in the art would produce the claimed invention by routine experimentation? If this rejection is to be maintained, for the record, the Applicants again respectfully request that the Examiner address this point specifically.

The Applicants respectfully submit that this rejection of the claims under 35 U.S.C. §103 has been adequately addressed. Withdrawal of this rejection is respectfully requested.

#### **Rejection under 35 U.S.C. §103 – Nippon**

Claims 1-2, 4-5, 8-9, 33, 35-36 and 39-40 are rejected under 35 U.S.C. §103(a) as unpatentable in view of Nippon. The Applicants respectfully traverse this rejection.

The Advisory Action indicates "Absent any evidence of the argued unexpected advantage or results, the claims remain rejected under 103." However, Applicants respectfully submit that such evidence was provided in Applicants amendment and response filed January 20, 2004, responsive to the Final Office Action dated October 17, 2003.

Specifically, in that response, Applicants submitted that the compositions possess an unexpected property, i.e., stability, that is not fairly taught or suggested in the cited art, and directed the Examiner's attention to specific parts of the instant specification which clearly evidence the unexpected properties. For example, these unexpected properties are best seen in Fig. 2 of the instant application, where results show that the claimed compositions are unexpectedly stable at 56°C for one week. Figure 2 shows that

the presence of FAD dramatically increase the stability of a signal producing system over a signal producing system in the absence of these compounds.

Accordingly, while the Advisory Action indicates that evidence to support these unexpected results has not been provided, Applicants respectfully submit that such evidence has been provided and in fact have directed the Examiner to the exact parts of the instant application where such evidence may be found. Because evidence of unexpected results has been provided, if this rejection is to be maintained Applicants respectfully request the Examiner to specify why the Examiner believes the submitted evidence is insufficient.

Finally, as noted in Applicants' previous filed response, the Office has attempted to establish these rejections by arguing that "at the time of the claimed invention it would have been well within the purview of one of ordinary skill in the art to optimize amounts of effective ingredients as a matter of routine experimentation" and "one of skill in the art would have been motivated by routine practice to optimize the reagents of ... with a reasonable expectation for successfully obtaining an effective reagent composition." However, the Office has not stated what would motivate one of skill in the art to add such large amounts of flavin/group III compounds to the prior art compositions and then test those compositions for increased stability. Without such motivation, Applicants respectfully ask why one of skill in the art would produce the claimed invention by routine experimentation? If this rejection is to be maintained, for the record, the Applicants again respectfully request that the Examiner address this point specifically.

The Applicants respectfully submit that this rejection of the claims under 35 U.S.C. §103 has been adequately addressed. Withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. §103 – Steinbach**

Claims 1, 2, 4, 6, 8, 33, 37 and 39 are rejected under 35 U.S.C. §103(a) as unpatentable in view of Steinbach. The Applicants respectfully traverse this rejection.

The Advisory Action indicates "Absent any evidence of the argued unexpected advantage or results, the claims remain rejected under 103." However, Applicants respectfully submit that such

evidence was provided in Applicants amendment and response filed January 20, 2004, responsive to the Final Office Action dated October 17, 2003.

Specifically, in that response, Applicants submitted that the compositions possess an unexpected property, i.e., stability, that is not fairly taught or suggested in the cited art, and directed the Examiner's attention to specific parts of the instant specification which clearly evidence the unexpected properties. For example, these unexpected properties are best seen in Fig. 2 of the instant application, where results show that the claimed compositions are unexpectedly stable at 56°C for one week. Figure 2 shows that the presence of FAD dramatically increase the stability of a signal producing system over a signal producing system in the absence of these compounds.

Accordingly, while the Advisory Action indicates that evidence to support these unexpected results has not been provided, Applicants respectfully submit that such evidence has been provided and in fact have directed the Examiner to the exact parts of the instant application where such evidence may be found. As such, Applicants respectfully submit that evidence of unexpected results has been provided. Because evidence of unexpected results has been provided, if this rejection is to be maintained Applicants respectfully request the Examiner to specify why the Examiner believes the submitted evidence is insufficient.

Finally, as noted in Applicants' previous filed response, the Office has attempted to establish these rejections by arguing that "at the time of the claimed invention it would have been well within the purview of one of ordinary skill in the art to optimize amounts of effective ingredients as a matter of routine experimentation" and "one of skill in the art would have been motivated by routine practice to optimize the reagents of ... with a reasonable expectation for successfully obtaining an effective reagent composition." However, the Office has not stated what would motivate one of skill in the art to add such large amounts of flavin/group III compounds to the prior art compositions and then test those compositions for increased stability. Without such motivation, Applicants respectfully ask why one of skill in the art would produce the claimed invention by routine experimentation? If this rejection is to be maintained, for the record, the Applicants again respectfully request that the Examiner address this point specifically.

The Applicants respectfully submit that this rejection of the claims under 35 U.S.C. §103 has been adequately addressed. Withdrawal of this rejection is respectfully requested.

**Rejection under 35 U.S.C. §103 – Geisler**

Claims 34, 35, 37, and 39-41 are rejected under 35 U.S.C. §103(a) as unpatentable in view of Geisler. The Applicants respectfully traverse this rejection.

The rejected claims are directed to compositions containing a Group III agent present at a molar ratio of about 50 to about 800.

The Advisory Action indicates “Absent any evidence of the argued unexpected advantage or results, the claims remain rejected under 103.” However, Applicants respectfully submit that such evidence was provided in Applicants amendment and response filed January 20, 2004, responsive to the Final Office Action dated October 17, 2003.

Specifically, in that response, Applicants submitted that the compositions possess an unexpected property, i.e., stability, that is not fairly taught or suggested in the cited art, and directed the Examiner’s attention to specific parts of the instant specification which clearly evidence the unexpected properties. For example, these unexpected properties are best seen in Fig. 1 of the instant application, where results show that the claimed compositions are unexpectedly stable at 56°C for one week. Figure 1 shows that the presence of borax dramatically increase the stability of a signal producing system over a signal producing system in the absence of these compounds.

Accordingly, while the Advisory Action indicates that evidence to support these unexpected results has not been provided, Applicants respectfully submit that such evidence has been provided and in fact have directed the Examiner to the exact parts of the instant application where such evidence may be found. As such, Applicants respectfully submit that evidence of unexpected results has been provided. Because evidence of unexpected results has been provided, if this rejection is to be maintained Applicants respectfully request the Examiner to specify why the Examiner believes the submitted evidence is insufficient.

Finally, as noted in Applicants’ previous filed response, the Office has attempted to establish these rejections by arguing that “at the time of the claimed invention it would have been well within the purview of one of ordinary skill in the art to optimize amounts of effective ingredients as a matter of routine experimentation” and “one of skill in the art would have been motivated by routine practice to



optimize the reagents of ... with a reasonable expectation for successfully obtaining an effective reagent composition.” However, the Office has not stated what would motivate one of skill in the art to add such large amounts of flavin/group III compounds to the prior art compositions and then test those compositions for increased stability. Without such motivation, Applicants respectfully ask why one of skill in the art would produce the claimed invention by routine experimentation? If this rejection is to be maintained, for the record, the Applicants again respectfully request that the Examiner address this point specifically.

The Applicants respectfully submit that this rejection of the claims under 35 U.S.C. §103 has been adequately addressed. Withdrawal of this rejection is respectfully requested.

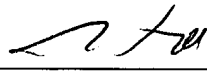
**CONCLUSION**

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number LIFE-040.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

Date: 3/17/04

By:   
Susan Tall  
Registration No. 52,272

BOZICEVIC, FIELD & FRANCIS LLP  
200 Middlefield Road, Suite 200  
Menlo Park, CA 94025  
Telephone: (650) 327-3400  
Facsimile: (650) 327-3231

F:\DOCUMENT\LIFE\040\Response to advisory action dated 2-13-04.doc